Remarks

Claims 1-25 are pending and under examination in the subject application. Applicants have also added new claims 26-29.

Applicants have hereinabove amended claims 4, 5, 7, 9, and 10, and added new claims 26-29. Applicants maintain that the amendments to claims 4, 5, 7, 9, and 10, and new claims 26-29 raise no issue of new matter. Support for the amendments to claim 4 can be found in the specification as originally filed at, *inter alia*, page 5, line 18 to page 6, line 2; page 13, lines 4-6; page 15, lines 7-14; and claim 4. Support for the amendments to claim 5 can be found in the specification as originally filed at, *inter alia*, page 5, lines 10-16; page 13, line 9; page 15, lines 7-14, and claim 5. Support for the amendments to claim 7 can be found in the specification as originally filed at, *inter alia*, page 15, lines 15-19; and claim 7. Support for the amendments to claim 9 can be found in the specification as originally filed at, *inter alia*, page 5, line 18 to page 6, line 2; page 15, lines 15-19; and claim 9. Support for the amendments to claim 10 can be found in the specification as originally filed at, *inter alia*, page 5, lines 10-16; page 13, line 9; page 15, lines 15-19; and claim 10. Support for new claim 26 can be found in the specification as originally filed at, *inter alia*, page 5, line 18 to page 6, line 2; page 13, lines 4-6; page 15, lines 7-14; page 17, lines 3-5; and claim 4. Support for new claim 27 can be found in the specification as originally filed at, *inter alia*, page 5, line 18 to page 6, line 2; page 13, lines 4-6; page 15, lines 7-14; page 17, lines 3-5; and claim 5. Support for new claim 28 can be found in the specification as originally filed at, *inter alia*, page 5, line 18 to page 6, line 2; page 13, line 9; page 15, lines 15-19; page 17, lines 3-5; and claim 9. Support for new claim 29 can be found in the specification as originally filed at, *inter alia*,

page 5, line 18 to page 6, line 2; page 13, line 9; page 15, lines 15-19; page 17, lines 3-5; and claim 10. Accordingly, applicants respectfully request entry of this Amendment. Upon entry of this Amendment claims 1-29 will be pending and under examination.

Restriction Requirement

In the March 18, 2005 Office Action, the Examiner required restriction to one of the following allegedly independent and distinct inventions characterized by the following Groups I-XII:

I. Claims 1-3, 6-8 and 11, as specifically drawn to a method for treatment of an apoptosis-related disease in a subject comprising administering an antibody;

II. Claims 1-2, 4-7 and 9-11, as specifically drawn to a method of treatment for an apoptosis-related disease in a subject comprising administering an nucleotides;

III. Claims 12 and 14, as specifically drawn to an antisense oligonucleotide having the sequence set forth in SEQ ID NO: 3;

IV. Claims 13-14, as specifically drawn to an antisense oligonucleotide having the sequence set forth in SEQ ID NO:4;

V. Claim 15, as specifically drawn to a process for determining the susceptibility of a subject to a chemotherapeutic treatment of an apoptosis-related disease comprising; determining the level of ATRX polypeptide in a healthy individual compared to a

subject;

VI. Claim 16, as specifically drawn to a process for determining the susceptibility of a subject to a chemotherapeutic treatment of an apoptosis-related disease comprising: determining the level of mRNA encoding the ATRX polypeptide in a healthy individual compared to a subject;

VII. Claim 17, as specifically drawn to a process for determining the efficacy of a chemotherapeutic treatment administered to a subject comprising: determining the level of the ATRX polypeptide prior to and after treatment, wherein a high level prior to treatment compared to after indicates the efficacy of treatment;

VIII. Claim 18, as specifically drawn to a process for determining the efficacy of a chemotherapeutic treatment administered to a subject comprising: determining the level of the ATRX mRNA in the subject prior to and after treatment, wherein a high level prior to treatment compared to after indicates the efficacy of the treatment;

IX. Claim 19, as specifically drawn to a process for diagnosing a cancer in a subject comprising: determining the level of ATRX polypeptide;

X. Claim 20, as specifically drawn to a process for diagnosing a cancer in a subject comprising: determining the level of polynucleotide encoding the ATRX polypeptide;

XI. Claims 21-22 and 24-25, as specifically drawn to a process for obtaining a compound which modulates apoptosis in a cell; and

XII. Claim 23, as specifically drawn to a process for obtaining a compound which promotes apoptosis in a cell.

On page 4 of the March 18, 2005 Office Action, the Examiner alleged that while the inventions of both Group III and Group IV are polynucleotides, in this instance the polynucleotide of Group III is 294 nucleotides in length, whereas the polynucleotide of Group IV is 296 nucleotides in length. The Examiner also alleged that the specification does not disclose that the two polynucleotides contain any structural similarity. The Examiner further alleged that the polynucleotides of Groups III and IV are structurally distinct molecules; any relationship between polynucleotides of Groups III and IV is dependent upon the correlation between the scope of the "sense" polynucleotide for which they are complementary to. The Examiner alleged that the polynucleotides are patentably distinct.

Further on page 4 of the March 18, 2005 Office Action, the Examiner alleged that searching the inventions of Group III and Group IV would impose a serious search burden since the search for two different polynucleotides, and different polynucleotide segments in the databases, in addition to searching the organic molecule databases would require extensive searching and review.

On page 4 of the March 18, 2005 Office Action, the Examiner alleged that the inventions of Groups I-II are unrelated. The Examiner alleged that in the instant case the specification does not disclose that their methods would be used together. The Examiner also alleged that the method for treating an apoptosis

related disease comprising administering an antibody (Group I), the method for treating an apoptosis related disease comprising administering an oligonucleotide (Group II) are unrelated as they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. The Examiner alleged that each invention performs this function using structurally and functionally divergent material, and therefore, each method is divergent in materials and steps. The Examiner further alleged that the distinct steps and products require separate and distinct searches. As such, it would be burdensome to search the inventions of Groups I-II.

On page 5 of the March 18, 2005 Office Action, the Examiner alleged that the inventions of Groups V-X are unrelated. The Examiner alleged that in the instant case, the specification does not disclose that their methods would be used together. The Examiner alleged that the process for determining the susceptibility of a subject to a chemotherapeutic treatment by detecting the change in ATRX polypeptide (Group V), the process for determining the susceptibility of a subject to a chemotherapeutic treatment by detecting the change in mRNA encoding the ATRX polypeptide (Group VI), the process for determining the efficacy of a chemotherapeutic treatment by determining the change in ATRX polypeptide (Group VII), the process for determining the efficacy of a chemotherapeutic treatment by determining the change in mRNA encoding the ATRX polypeptide (Group VIII), the process for diagnosing cancer in a subject by determining the level of ATRX polypeptide (Group XI), and), the process for diagnosing cancer in a subject by determining the level of mRNA that encodes the ATRX polypeptide (Group X) are unrelated as they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. The Examiner alleged that each

invention performs this function using structurally and functionally divergent material and that the methodology and materials necessary for determining differ significantly for each of the materials.

On page 5 of the March 18, 2005 Office Action, the Examiner alleged that the inventions of Groups XI and XII are unrelated. The Examiner alleged that in the instant case, the specification does not disclose that their methods would be used together. The Examiner alleged that the process for obtaining a compound which modulates apoptosis in a cell (Group XI) and the process for obtaining a compound which promotes apoptosis in a cell (Group XII) are unrelated as they comprise different steps and utilize different products which demonstrates that each method has a different mode of operation. The Examiner further alleged that each invention performs this function using structurally and functionally divergent material, and that the methodology and materials necessary for obtaining a compound differ significantly for each of the materials. The Examiner alleged that for obtaining a compound which modulates apoptosis, a cell expressing ATRX polypeptide is contacted with a compound, wherein the compound may be an agonist or an antagonist. The Examiner alleged that for obtaining a compound which promotes apoptosis, a control cell is treated with an apoptosis-stimulating agent which causes apoptosis in the control and not in the test. The Examiner alleged that each method is divergent in materials and steps and for these reasons the inventions of Groups XI and XII are patentably distinct.

In response, applicants hereby elect, with traverse, the invention of the claims 1, 2, 5, 6, 7, 10, and 11 drawn to a method of treatment for an apoptosis related disease in a subject comprising administering an siRNA.

Applicants respectfully request that the Examiner reconsider and withdraw the restriction requirement. Under 35 U.S.C. §121, restriction may be required if two or more independent and distinct inventions are claimed in one application.

Under M.P.E.P. §802.01, "independent" means there is no disclosed relationship between the subjects disclosed. The inventions of Groups I-II are both drawn to methods of treating an apoptosis-related disease in a subject by administering an inhibitor of the ATRX polypeptide. Groups III-IV are both drawn to inhibitors of the ATRX polypeptide. Groups V-VI are drawn to methods of determining susceptibility of a subject to chemotherapeutic treatment of an apoptosis-related disease by comparing levels of ATRX polypeptide or ATRX mRNA. Groups VII-VIII are drawn to methods of determining efficacy of treatment of an apoptosis-related disease in a subject by comparing levels of ATRX polypeptide or ATRX mRNA. Groups IX and X are drawn to methods of diagnosis cancer in a subject by determining the levels of ATRX polypeptide or polynucleotide in a subject. Groups XI and XII are drawn to processes for obtaining compounds that modulate or promote apoptosis in either a cell expressing the ATRX polypeptide or measuring their effect on the activity of the ATRX polypeptide. Applicants therefore maintain that the claims of Groups I-XII are not independent.

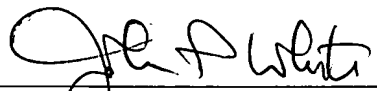
Furthermore, under MPEP §803, there are two criteria for a proper restriction requirement: 1) the invention must be independent or distinct (discussed above), and 2) there must be a serious burden on the Examiner if restriction is required. MPEP §803 unambiguously provides that "[i]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes

claims to independent and distinct inventions." Applicants respectfully submit that there would not be a serious burden on the Examiner if restriction is not required between Groups I-XII. A search for prior art material to the patentability of the claims 1, 2, 5, 6, 7, 10, and 11 drawn to a method of treatment for an apoptosis-related disease in a subject comprising administering an siRNA, would necessarily turn up prior art material to the patentability of the claims of Groups I-XII. Any search for treating an apoptosis-related disease using an inhibitor of the ATRX polypeptide will turn up other inhibitors of the ATRX polypeptide, other methods of treatment, and methods of diagnosis using the ATRX polypeptides. Since there is no burden on the Examiner to examine the elected claims 1, 2, 5, 6, 7, 10, and 11 Groups I-XII together in the subject application, it is therefore resubmitted that Groups I-XII should be examined on the merits.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the fee of $225.00 for a two-month extension of time and the fee of $100.00 for additional claims which are enclosed in a check for $325.00, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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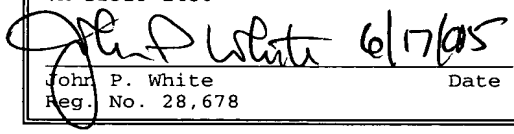
I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450



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